SECTION III
REMARKS

A. Regarding the Amendments

The specification has been amended to add sequence identifiers, where necessary. No new matter has been added, as defined by 35 U.S.C. § 132.

Claims 1, 5, 6, 9, 11, 14, and 17-19 have been amended as set forth in the above Complete Listing of the Claims.

New claims 20-30 have been added.

As amended, the claims are supported by the specification and the original claims. No new matter has been added, as defined by 35 U.S.C. § 132.

By the present amendment, cancellation of claims 4 and 7 is requested, without prejudice.

Thus, upon entry of the amendments, claims 1-3, 5, 6, and 8-30 will be pending, of which claims 15-17 are withdrawn.

B. Information Disclosure Statement

In the March 20, 2007 Office Action, the examiner indicates that the Information Disclosure Statement filed by the Applicants on October 14, 2004 fails to comply with the provisions of 37 C.F.R. §1.97, 1.98 and MPEP § 609 because translations of several foreign references were not provided. The references were identified as "AA", "AD" and "AG" on the October 14, 2004 Information Disclosure Statement.

The references previously identified as "AA" (WO 03/006065A2), "AD" (WO 01/05432 A2), and "AG" (DE 199 33 492 A1) are again listed on the attached PTO/SB/08a, and translations of these documents are provided. Specifically, U.S. Patent No. 6,821,948 is a translation of WO 01/05432 A2 and DE 199 33 492 A1 is the priority document to WO 01/05432 A2, the content of which does not go beyond U.S. Patent No. 6,821,948. Also provided is an English version of WO 03/006065 A2. It is respectfully requested that the information be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is being filed more than three months after the U.S. filing date and after the mailing date of the first Office Action on the merits, but before the mailing date of a Final Rejection or Notice of Allowance. Attached is credit card authorization form in the amount of $180.00 in payment of the fee under 37 C.F.R. §1.17(p).

C. Nucleotide Sequence and/or Amino Acid Sequence Disclosure

The examiner states that the sequence listing of the present application fails to comply with the requirements set forth in 37 C.F.R. §1.821(d) because the specification and drawings contain nucleic acid and amino acid sequences that are not accompanied by the required sequence identifiers.

By applicants' review, all sequences included in the application are included in the Sequence Listing filed with the USPTO on December 20, 2004. Specifically, the sequences on pages 6 and 10 are SEQ ID NOs: 1 and 2. The sequence set forth in Fig. 2 is SEQ ID NO: 3. The eight sequences set forth in Fig. 3(1) are SEQ ID NOs: 24-31, the eight sequences set forth in Fig.3(2) are SEQ ID NOs: 4-11, the nine sequences set forth in Fig. 3(3) are SEQ ID NOs: 11-19, the three sequences set forth in Fig. 3(4) are SEQ ID NOs: 20-22 and the sequence set forth in Fig. 3(5) is SEQ ID NO: 23. No additional sequences are found in the application.

As set forth above in Section I, Amendments to the Specification, sequence identifiers have been added to the specification, where necessary.

If it is the examiner's position that additional sequences are provided in the specification and/or drawings, that are not included in the 31 sequences of the Sequence Listing filed on December 20, 2004, specific identification of such sequences is requested.

Accordingly, applicant maintains that the application, as amended, complies with the requirements of 37 C.F.R. §§ 1.821-1.825

D. Rejection of Claim 14 Under 35 USC §112

In the March 20, 2007 Office Action, the examiner rejected claim 14 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Specifically, the examiner rejects to the language in claim 14 "for which the prokaryote was re-sensitized by administering the conjugate," stating that there was no antecedent basis for this language. As amended, claim 14 no longer contains this language, and amended claim 14 is fully supported by the language of previously pending claims 1, 13 and 14.

As such, claim 14 is definite within the requirements of 35 U.S.C. §112, second paragraph. Removal of the rejection is respectfully requested.

E. Right of Priority

The examiner has stated that applicants cannot rely on the foreign priority papers to overcome any rejection because a translation of the papers has not been made of record. In the original filing of the present application, applicants claimed priority under 35 U.S.C. §119 to PCT application PCT/DE03/00124 with a filing date of January 17, 2003 and to German patent application 10201862.6 with a filing date of January 18, 2002. As such, applicants claim a priority date of January 18, 2002. With the original filing of the present application under 35 U.S.C. §371, a copy of the PCT International Application and a translation of the PCT application were provided.

However, in accordance with the examiner's request, a translation of German patent application DE 102 01 862.6 is provided, along with a Declaration of Ursula Scherz that the English translation is "a true and correct translation."

Accordingly, applicants again assert a priority date of January 18, 2002 for the present application.

F. Rejection of Claims Under 35 U.S.C. §102

Claims 1-4, 13 and 18 were rejected under 35 U.S.C. §102(b) as being anticipated by Good et al. (Nature Biotechnology Vol. 19:360-364, April 2001; hereinafter "Good et al."). Applicants respectfully disagree.

Anticipation of a claim requires the disclosure in a single prior art reference of each element of the claim under consideration. (In re Spada, 15 USPQ2d 1655 (Fed. Cir., 1990), In re Bond, 15

USPQ2d 1566 (Fed. Cir., 1990). It is submitted that Good et al. do not disclose all elements of the claimed invention.

Good et al. disclose peptide-PNA conjugates targeted to the RNA of a gene (see abstract, Fig. 1, page 362, left column, 2nd paragraph), wherein the transport peptide $(KFF)_3K$ does not show antibacterial activity (page 361, left column, 2nd paragraph, lines 10 to 11). The present claims, in contrast, are drawn to conjugates composed of an antibacterial peptide or protein and a PNA directed against a DNA of a gene giving antibiotic resistance. Thus, Good et al. do not disclose the claimed elements of the present invention. Accordingly, withdrawal of the rejection of claims 1-4, 13 and 18 under 35 U.S.C. §102(b) as being anticipated by Good et al. is respectfully requested.

Additionally, claims 1-4, 7-9, 13, 14, 18 and 19 were rejected under 35 U.S.C. §102(e) as being anticipated by Nielsen et al. (U.S. 6,548,651; hereinafter "Nielsen et al.").

Nielsen et al. disclose peptide-PNA conjugates, wherein the PNA is an antisense PNA (col. 5, lines 53 to 67) and, in particular,

> "*infectious diseases are caused by micro-organisms including bacteria, viruses, protozoa, worms and arthropods. PNA can be modified and used to target RNA in such microorganisms, whether the micro-organisms are sensitive or resistant to antibiotics*" (col. 9, lines 61 to 65).

Nielsen et al. therefore teach an antisense therapy, wherein the mRNA is targeted, thereby inhibiting the translation of the mRNA to protein. On the contrary, the claimed subject-matter refers to an anti-gene therapy, wherein the DNA is targeted and the transcription of the DNA to mRNA is inhibited. Nielsen et al. do not teach or disclose to modify a PNA to target DNA, especially not to target "a DNA of a gene giving antibiotic resistance and inhibiting the transcription of this gene" such as is recited in claim 1 of the present invention, from which rejected claims 2-4, 7-9, 13, 14, 18, and 19 depend.

Therefore, claims 1-4, 7-9, 13, 14, 18 and 19 are novel over Nielsen et al. and withdrawal of the rejection of claims 1-4, 7-9, 13, 14, 18 and 19 under 35 U.S.C. §102(e) as being anticipated by Nielsen et al. is respectfully requested.

F. Rejection of Claims Under 35 U.S.C. §103

Claims 1-14, 18 and 19 were rejected under 35 U.S.C. §103(a) in the March 20, 2007 Office Action, as being unpatentable over Nielsen et al., Good et al. and Rothbard et al. (WO 98/52614; hereinafter "Rothbard et al."), in view of Bernhardt et al. (Research in Microbiology, Vol. 153:493-501, 2002; hereinafter "Bernhardt et al.") and Yu et al. (cited in Applicants' October 14, 2004 IDS; hereinafter "Yu et al."), Good et al. (Nature Biotechnology, Vol. 16:355-358; hereinafter "Good et al. (2)") and Braun et al. (U.S. 6,821,948; hereinafter "Braun et al."). Initially, it is noted that Bernhardt et al. was published on June 11, 2002, which is after the priority date of January 18, 2002 of the present application. Thus, Bernhardt et al. is not eligible as prior art to the present application. Accordingly, the rejection under 35 U.S.C. §103(a) will be discussed below as a rejection over Nielsen et al., Good et al. and Rothbard et al. in view of Yu et al. Good et al. (2) and Braun et al.

It is elemental law that in order for an invention to be obvious, the difference between the subject matter of the application and the prior art must be such that the subject matter as a whole would have been obvious at the time the invention was made to a person of ordinary skill in the art. In order to meet this standard for a proper §103 rejection, all claim limitations must be disclosed or derivable from the cited combination of references, there must be a logical reason to combine the cited references to produce an operable combination. See MPEP §2143:

> **"2143 Basic Requirements of a Prima Facie Case of Obviousness**
>
> "To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.
>
> "The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)."

The claimed invention recites to a dual strategy of providing a conjugate which is generally toxic to bacteria by virtue of the antibacterial transport peptide, on the one hand, and, on the other

hand, introduces a PNA directed specifically against the DNA of a gene giving antibiotic resistance in order to resensitize the bacteria to an antibiotic against which they were previously resistant.

The therapeutic approach of the present invention is distinguished from that of the cited prior art due to targeting the PNA to the DNA of the gene and, thereby, inhibiting the transcription of the gene. Hence, the expression of the gene giving antibiotic resistance is inhibited from the start, as further proliferation of the pathogen is immediately stopped and inactivated, effectively. Such action is particularly favorable for *in vivo* applications. However, if, as in the antisense approaches of the cited prior art, gene expression is inhibited at the translational level by targeting the mRNA, then transcription of the gene continues, thereby synthesizing mRNA *de novo* which may require additional amounts of the agent to inhibit the gene expression.

The relevant disclosure of Nielsen et al. is discussed above with regard to the rejection under 35 U.S.C. §102. In particular, Nielsen et al. describe targeting RNA in microorganisms (see col. 9, lines 61 to 65). Therefore, Nielsen et al. do not describe a conjugate such as that recited in the present application, which comprises targeting the DNA of a gene giving antibiotic resistance.

Good et al. (2001) is also discussed above with regard to the rejection under 35 U.S.C. §102. Like Nielsen et al., Good et al. describe targeting of the mRNA of the *lacZ* gene or the *acpP* gene. Moreover, Good et al. describe use of a transport peptide which is not antibacterial (see page 361, left column, 2nd paragraph, line 10). Good et al. do not describe a conjugate such as that recited in the present application, which comprises an antibacterial transport and a PNA targeting the DNA of a gene giving antibiotic resistance.

Similarly, Good et al. (2) (1998) describe PNA targeting the start codons of the ß-galactosidase and ß-lactamase genes at the translation level, i.e. the mRNA (see page 355, right column, 2nd paragraph, in particular last sentence). Good et al. do not describe a conjugate such as that recited in the present application, targeting the DNA of a gene giving antibiotic resistance.

Rothbard et al. generally describe peptide-conjugates containing antimicrobial agents that may be used in preventing microbial infection (e.g. page 17, lines 25-28). Rothbard et al. do not describe either antibacterial transport peptides or PNA's targeting genes giving antibiotic resistance.

As cited by the examiner, Bernhardt et al. and Yu et al. were cited only to show that phage-holin and defensin polypeptides were known at the time of the invention. However, combination of these references with the additionally cited references fails to provide derivative basis for an assertion of obviousness of the claimed invention.

As discussed above, none of the cited references alone provides description of the various elements of the claimed invention. Accordingly, in combination, Nielsen et al., Good et al. and Rothbard et al. in view of Yu et al. Good et al. (2) and Braun et al. fail to provide any derivative basis for a conjugate such as that recited in the present application, which comprises an antibacterial transport and a PNA targeting the DNA of a gene giving antibiotic resistance. Accordingly, no basis of *prima facie* obviousness of the claimed invention is presented by such cited references.

As Nielsen et al., Good et al. and Rothbard et al. in view of Yu et al. Good et al. (2) and Braun et al. do not provide any logical basis for the conjugate recited in claims 1-14, 18 and 19, Nielsen et al., Good et al. and Rothbard et al. in view of Yu et al. Good et al. (2) and Braun et al. do not render the claimed invention obvious. Accordingly, withdrawal of the rejection of claims 1-14, 18 and 19 under 35 U.S.C. § 103 (a) as being obvious over Nielsen et al., Good et al. and Rothbard et al. in view of Yu et al. Good et al. (2) and Braun et al. is respectfully requested.

G. Fees Due

The time for responding to the March 20, 2007 Office Action without extension was set at three months, or June 20, 2007. Applicants hereby request a one (1) month extension of time under 37 C.F.R. § 1.136 to extend the deadline for response to and including July 20, 2007. Payment of the extension fee of $60.00 specified in 37 C.F.R. § 1.17(a)(i), as applicable to small entity, is authorized by the enclosed Credit Card Payment Form PTO-2038.

New claims 20-30 have been added to the pending application by the present amendment. The currently pending claims of the application include 2 independent claims and 28 total claims. As 1 independent claim and 19 total claims have been previously presented and paid for in this application, the present amendment provides authorization for additional claims fees of $200.00 (0 independent claims in excess of 3 and 8 (x $25) total claims in excess of 20), as applicable to small entity, provided for on the enclosed Credit Card Payment Form PTO-2038.

Also included with the present response is an Information Disclosure Statement being filed more than three months after the U.S. filing date AND after the mailing date of the first Office Action on the merits, but before the mailing date of a Final Rejection or Notice of Allowance. Accordingly, the required fee under 37 C.F.R. §1.17(p) is $180.00 , which is authorized by the enclosed Credit Card Payment Form PTO-2038.

Accordingly, the total fees authorized by the enclosed Credit Card Payment Form PTO-2038 is $440.00, which includes $60.00 for a one month extension of time, $ 200.00 in additional claims fees and $180.00 for filing of the Information Disclosure Statement.

CONCLUSION

Based on the foregoing, all of Applicants' pending claims 1-3, 5, 6, and 8-14, 18-30 are patentably distinguished over the art, and are in form and condition for allowance. The Examiner is requested to favorably consider the foregoing and to responsively issue a Notice of Allowance.

The fees due with regard to the filing of this paper total $ 440.00, as detailed in Section H above. Payment of such fees is authorized by the enclosed Credit Card Payment Form PTO-2038. Should any additional fees be required or an overpayment of fees made, please debit or credit our Deposit Account No. 08-3284, as necessary.

If any issues require further resolution, the Examiner is requested to contact the undersigned attorney at (919) 419-9350 to discuss same.

Respectfully submitted,

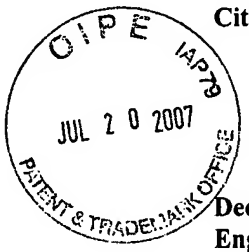
Date: July 20, 2007

Steven J. Hultquist
Reg. No. 28,021
Attorney for Applicants

Date: July 20, 2007

Kelly K. Reynolds
Reg. No. 51,154
Attorney for Applicants

INTELLECTUAL PROPERTY/
TECHNOLOGY LAW
Phone: (919) 419-9350
Fax: (919) 419-9354
Attorney File No.: 4121-170



Enclosures:
Form PTO/SB/08a [1 pg.]
Cited References:
US 6,821,948 B1[18 pgs.]
WO 03/006065 A2 [30 pgs.]
English Translation of WO 03/006065 A2 [13 pgs.]
WO 01/05432 A2 [26 pgs]
DE 199 33 492 A1 [10 pgs.]
Declaration of Ursula Schertz [1 pg.]
English translation of priority document [31 pgs.]
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